Palladium-catalysed direct Amination of 2,3-Dihydrofuran by Morpholine

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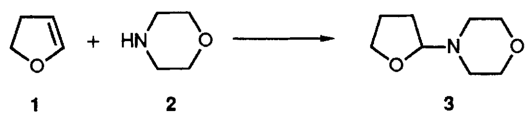
The first palladium-catalysed condensation of an amine with an alkene has been observed on 2,3-dihydrofuran and morpholine with 45 turnovers.

The direct amination of alkenes to produce the corresponding alkylamine represents a fascinating challenge. Except for the condensation of aniline to norbornene with four turnovers catalysed by $[Ir(PEt_3)_2(C_2H_4)_2Cl]$,[1] the only case described in the literature where this reaction was readily catalysed was restricted to ethylene and secondary amines in the presence of rhodium or iridium trichloride.[2] Many explorations have been published, essentially by the Hegedus and Åkermark's research groups on various palladium complexes, but the reaction remains stoichiometric since a hydrogenolysis step was necessary to produce the expected amine.[3,4] We now report that modifications of the palladium coordination sphere gives access to catalyst precursors active for the amination of 2,3-dihydrofuran **1** by morpholine **2** under ambient conditions (Scheme 1).

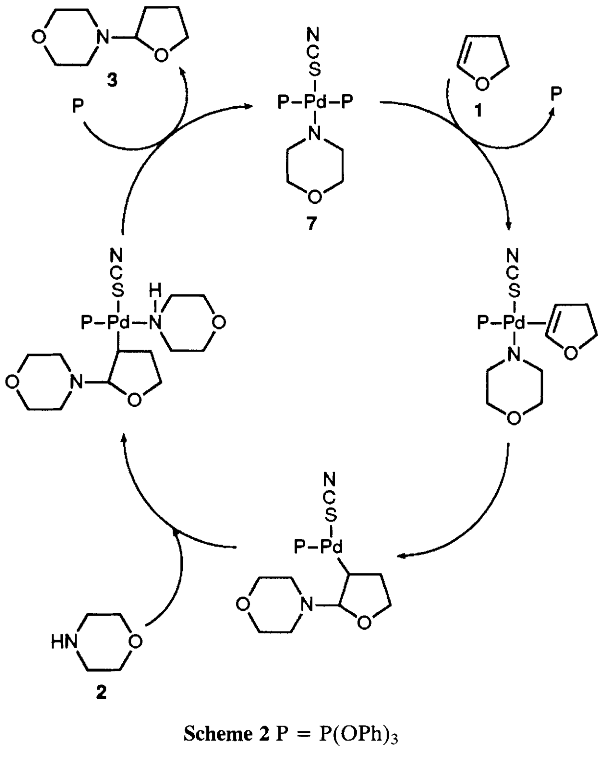
Since the hydrogenolysis step produces a hydridochloropalladium complex, which is unstable and gives metallic palladium and hydrogen chloride, our strategy was to synthesize compounds in which the chloro anion would be replaced by a soft basic anion, *i.e.* to have a weak HX acid instead of HCl. Thus, we prepared the two complexes $[Pd(SCN)_2\{P(OPh)_3\}_2]$ **4** and $[Pd(NCS)_2(PPh_3)_2]$ **5**.[5]



Catalyst precursors: $[Pd(SCN)_2\{P(OPh)_3\}_2]$, $[Pd(NCS)_2(PPh_3)_2]$
4 **5**

Scheme 1

The addition of diethylamine or morpholine **2** to oct-1-ene as a representative substrate of non-activated alkenes was not accomplished in various solvents, even in refluxing toluene for one day.



Scheme 2 P = $P(OPh)_3$

Morpholine was shown to react with 2,3-dihydrofuran whose vinyl ether structure allows for a slightly activated carbon–carbon bond. The two complexes **4** and **5** catalyse the synthesis of **3**. For instance, 5.73 mmol (6 ml) of **2** were added dropwise at room temperature to a solution containing 66 mmol of **1** and 0.127 mmol of **4**. Full conversion of **2** was achieved within 15 h. Compound **3** was the sole product obtained during this reaction as shown by gas chromatography coupled with mass spectrometry as well as by ^{1}H and ^{13}C NMR spectroscopy.† Thus, 45 turnovers characterize this novel catalytic system.

Preliminary investigation was carried out to have some insight into the catalytic cycle, based on complex **4**, complex **5**, being less soluble. In particular morpholinium thiocyanate $[\overline{CH_2CH_2OCH_2CH_2N}H_2][SCN]$ **6** was identified‡ together with a palladium main complex§ which contains a thiocyanato ligand, two phosphite ligands and a tentatively assigned amido group. Thus, complex $[Pd(SCN)\{\overline{NCH_2CH_2OCH_2CH_2}\}\{P(OPh)_3\}_2]$ **7** would be formed simultaneously to **6** by addition of morpholine to the starting complex **4**. Some amounts of a complex containing a hydride and a morpholine ligand have been detected.¶ We propose a catalytic cycle, delineated in Scheme 2, where an intrasphere nucleophilic attack of the amido group occurs on the coordinated alkene.

Work is in progress to generalize this reaction as well as to understand its intimate mechanism.

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† Compound **3**: mass spectrum (EI) *m/z* 157 (M^+), 156 ($M^+ - H$), 127 ($M^+ - HCHO$), 112 ($127 - CH_2$), 100 ($127 - C_2H_4$), 99 ($112 - CH_2$), 86 ($M^+ - \overline{CH_2CH_2CH_2{\cdot}C}HO$), 71 ($99 - C_2H_4$) and ($M^+ - \overline{CH_2CH_2{\cdot}NCH_2C}H_2O$), 57 ($86 - HCHO$), 41 ($71 - HCHO$), 28 ($57 - C_2H_4$). *Selected spectroscopic data,* ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.5 (1H C-2 of furyl); ^{13}C NMR (60 MHz, $CDCl_3$) δ 96 (doublet J_{CH} 157.7 Hz, C-2).

‡ Compound **6**: *selected spectroscopic data*, IR ν/cm^{-1} (KBr) ν_{NH} 3400, ν_{CN} 2077 (free SCN^- as in KSCN), ν_{COC} 1109 (morpholine ring); ^{1}H NMR (200 MHz, [$^2H_6$]dimethyl sulfoxide: δ 3.2 (triplet, NCH_2 from morpholine), δ 3.88 (triplet, OCH_2 from morpholine) to compare with $[\overline{CH_2CH_2OCH_2CH_2N}H_2][HSO_4]$ δ 3.0 (triplet, NCH_2 from morpholine), δ 3.75 (triplet, OCH_2 from morpholine). The NH signals have been detected at δ 9.0 and 3.8 (broad signals) respectively.

§ Compound **7**: *selected spectroscopic data*, IR ν/cm^{-1} (KBr), ν_{CN} 2155, ν_{COC} 1109, ^{1}H NMR (200 MHz; $CDCl_3$): δ 3 (4H NCH_2 from morpholine), δ 3.75 (4H OCH_2 from morpholine), δ 7.2 (PPh_3); ^{13}C NMR (60 MHz; $CDCl_3$): δ 43.9 (NCH_2 from morpholine), δ 63.8 (OCH_2 from morpholine).

¶ *Selected spectroscopic data,* ^{1}H NMR (200 MHz, CD_3COCD_3) δ −16.8 (Pd–H).